Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1-26 (cancelled)

27. (currently amended) A method for designing an optimized multi-epitope polypeptide comprising:

(i) selecting five ~~two~~ or more epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class I cytotoxic T lymphocyte (CTL) epitopes;

(ii) sorting said five or more epitopes to minimize the number of junctional epitopes, and

(iii) ~~(ii)~~ incorporating said five ~~two~~ or more CTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (iii) ~~(ii)~~:

at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said five ~~two~~ or more CTL epitopes; wherein said flanking or spacer amino acid residue is selected from the group consisting of lysine (K), arginine (R), asparagine (N), glutamine (Q), glycine (G), alanine (A), serine (S), cysteine (C), and threonine (T)~~; and~~

~~wherein said flanking or spacer amino acid residue prevents the occurrence of a CTL junctional epitope~~.

28. (currently amended) A method for designing an optimized multi-epitope polypeptide comprising:

(i) selecting two or more epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class II helper T lymphocyte (HTL) epitopes;

(ii) sorting said two or more epitopes to minimize the number of junctional epitopes, and

(iii) ~~(ii)~~ incorporating said two or more HTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (iii) ~~(ii)~~:

at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitopes; wherein said flanking or spacer amino acid residue is selected from the group consisting of glycine (G) [[G]], proline (P), asparagine (N) [[N]] or alanine (A) ~~A; and~~

~~wherein said flanking or spacer amino acid residue prevents the occurrence of an HTL junctional epitope~~.

29. (previously presented) The method of claim 28, wherein said flanking or spacer amino acid residues are independently selected from residues that are not known human leukocyte antigen (HLA) Class II primary anchor residues.

30. (currently amended) The method of claim 28, wherein said flanking or spacer amino acid residues comprise at least 5 amino acid residues independently selected from the group consisting of glycine (G), proline (P) and asparagine (N) ~~G, P, and N~~.

31. (currently amended) The method of claim 30, wherein said flanking or spacer amino acid residues are glycine-proline-glycine-proline-glycine (GPGPG) ~~GPGPG~~ (SEQ ID NO: 369).

32. (currently amended) The method of claim 27, wherein said flanking or spacer amino acid residues comprise 1, 2, 3, 4, 5, 6, 7, or 8 amino acid residues selected from the group consisting of alanine (A) and glycine (G) ~~A and G~~.

33. (cancelled)

34. (currently amended) The method of claim 27, wherein said flanking or spacer amino acid residues are selected from the group consisting of lysine (K), arginine (R), asparagine (N), glycine (G) and alanine (A) ~~K, R, N, G, and A~~.

35. (cancelled)

36. (currently amended) The method of claim 27, further comprising substituting an N-terminal residue of an HLA epitope that is adjacent to a C-terminus of an HLA epitope comprised by the multi-epitope polypeptide with a residue selected from the group consisting of lysine (K), arginine (R), asparagine (N), glycine (G) and alanine (A) ~~K, R, N, G, and A~~.

37-58. (cancelled)

59. (previously presented) The method of claim 27, further comprising:

(i) introducing the multi-epitope polypeptide into a cell; and

(ii) determining that the multi-epitope polypeptide is processed by an HLA processing pathway such that all of the epitopes included in the multi-epitope polypeptide are produced by an HLA processing pathway.

60.-61. (cancelled)

62. (currently amended) The method of claim 27, further comprising:

(i) selecting two or more epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class II helper T lymphocyte (HTL) epitopes; and

(ii) incorporating said two or more HTL epitopes into said ~~a~~ multi-epitope polypeptide, wherein, during the incorporation step (ii):

at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitopes; wherein said flanking or spacer amino acid residue is selected from the group consisting of glycine (G), proline (P), asparagine (N) or alanine (A) ~~G, P, N or A; and~~

~~wherein said flanking or spacer amino acid residue prevents the occurrence of an HTL junctional epitope~~.

63. (currently amended) The method of claim 28, further comprising:

(i) selecting two or more epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class I cytotoxic T lymphocyte (CTL) epitopes; and

(ii) incorporating said two or more CTL epitopes into said ~~a~~ multi-epitope polypeptide, wherein, during the incorporation step (ii):

at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitopes; wherein said flanking or spacer amino acid residue is selected from the group consisting of lysine (K), arginine (R), asparagine (N), glutamine (Q), glycine (G), alanine (A), serine (S), cysteine (C) and threonine (T) ~~K, R, N, Q, G, A, S, C, and T; and~~

~~wherein said flanking or spacer amino acid residue prevents the occurrence of a CTL junctional epitope~~.

64. (previously presented) The method of claim 27, wherein said multi-epitope polypeptide contains 10 or more CTL epitopes.

65. (previously presented) The method of claim 64, wherein said multi-epitope polypeptide contains 20 or more CTL epitopes.

66. (previously presented) The method of claim 65, wherein said multi-epitope polypeptide contains 30 or more CTL epitopes.

67. (previously presented) The method of claim 66, wherein said multi-epitope polypeptide contains 40 or more CTL epitopes.

68. (previously presented) The method of claim 28, wherein said multi-epitope polypeptide contains 10 or more HTL epitopes.

69. (previously presented) The method of claim 68, wherein said multi-epitope polypeptide contains 20 or more HTL epitopes.

70. (previously presented) The method of claim 69, wherein said multi-epitope polypeptide contains 30 or more HTL epitopes.

71. (previously presented) The method of claim 70, wherein said multi-epitope polypeptide contains 40 or more HTL epitopes.

72. (currently amended) A method for designing a polynucleotide encoding an optimized multi-epitope polypeptide comprising:

(i) selecting five ~~two~~ or more nucleic acid sequences which encode epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class I cytotoxic T lymphocyte (CTL) epitopes;

(ii) sorting said five or more nucleic acid sequences to minimize the number of encoded junctional epitopes, and

(iii) ~~(ii)~~ incorporating said five ~~two~~ or more CTL epitope-encoding nucleic acid sequences into a multi-epitope polynucleotide, wherein, during the incorporation step (iii) ~~(ii)~~:

a polynucleotide encoding at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said five ~~two~~ or more CTL epitope-encoding nucleic acid sequences; wherein said flanking or spacer amino acid residue is selected from the group consisting of lysine (K), arginine (R), asparagine (N), glutamine (Q), glycine (G), alanine (A), serine (S), cysteine (C) and threonine (T) ~~K, R, N, Q, G, A, S, C, and T; and~~

~~wherein said flanking or spacer amino acid residue prevents the occurrence of a CTL junctional epitope~~.

73. (currently amended) A method for designing a polynucleotide encoding an optimized multi-epitope polypeptide comprising:

(i) selecting two or more nucleic acid sequences which encode epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class II helper T lymphocyte (HTL) epitopes;

(ii) sorting said two or more nucleic acid sequences to minimize the number of encoded junctional epitopes, and

(iii) ~~(ii)~~ incorporating said two or more HTL epitope-encoding nucleic acid sequences into a multi-epitope polynucleotide, wherein, during the incorporation step (iii) ~~(ii)~~:

polynucleotide encoding at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitope-encoding nucleic acid sequences; wherein said flanking or spacer amino acid residue is selected from the group consisting of glycine (G), proline (P), asparagine (N) or alanine (A) ~~G, P, N or A; and~~

~~wherein said flanking or spacer amino acid prevents the occurrence of an HTL junctional epitope~~.

74. (previously presented) The method of claim 28, further comprising:

(i) introducing the multi-epitope polypeptide into a cell; and

(ii) determining that the multi-epitope polypeptide is processed by an HLA processing pathway such that all of the epitopes included in the multi-epitope polypeptide are produced by an HLA processing pathway.

75.-76. (cancelled)

77. (currently amended) The method of claim 72, further comprising:

(i) selecting two or more nucleic acid sequences which encode epitopes that contain HLA allele-specific motifs or supermotifs, wherein said epitopes are human leukocyte antigen (HLA) class II helper T lymphocyte (HTL) epitopes; and

(ii) incorporating said two or more HTL epitope-encoding nucleic acid sequences into said ~~a~~ multi-epitope polynucleotide, wherein, during the incorporation step (ii):

a polynucleotide encoding at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitope-encoding nucleic acid sequences; wherein said flanking or spacer amino acid residue is selected from the group consisting of glycine (G), proline (P), asparagine (N) or alanine (A) ~~G, P, N or A; and wherein said flanking or spacer amino acid residue prevents the occurrence of an HTL junctional epitope~~.

78. (currently amended) The method of claim 73, further comprising:

(i) selecting two or more nucleic acid sequences which encode epitopes that contain HLA allele-specific motifs or supermotifs, wherein said epitopes are human leukocyte antigen (HLA) class I helper T lymphocyte (CTL) epitopes; and

(ii) incorporating said two or more CTL epitope-encoding nucleic acid sequences into said ~~a~~ multi-epitope polynucleotide, wherein, during the incorporation step (ii):

a polynucleotide encoding at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitope-encoding nucleic acid sequences; wherein said flanking or spacer amino acid residue is selected from the group consisting of lysine (K), arginine (R), asparagine (N), glutamine (Q), glycine (G), alanine (A), serine (S), cysteine (C) and threonine (T) ~~K, R, N, Q, G, A, S, C, and T; and wherein said flanking or spacer amino acid prevents the occurrence of a CTL junctional epitope~~.

79.-80. (cancelled)

81. (new) The method of claim 72, wherein said flanking or spacer amino acid residues are selected from the group consisting of lysine (K), arginine (R), asparagine (N), glycine (G) and alanine (A).

82. (new) The method of claim 73, wherein said flanking or spacer amino acid residues comprise at least 5 amino acid residues independently selected from the group consisting of glycine (G), proline (P) and asparagine (N).

83. (new) The method of claim 73, wherein said flanking or spacer amino acid residues are glycine-proline-glycine-proline-glycine (GPGPG) (SEQ ID NO: 369).